CLAIMS

1. A composition comprising a nucleic acid sequence and a hyaluronic acid or a derivative thereof, together with a pharmaceutically-acceptable carrier, wherein the nucleic acid is either an anti-sense nucleic acid directed against a target sequence or a sense nucleic acid encoding a desired protein.

2. A composition according to Claim 1, in which the nucleic acid is a nucleotide sequence which is in the anti-sense orientation to a target sequence.

3. A composition according to Claim 2, in which the target nucleic acid sequence is a genomic DNA, a cDNA, a messenger RNA or an oligonucleotide.

4. A composition according to Claim 1, in which the nucleic acid is present in a vector comprising a nucleic acid sequence to be transferred into a target cell.

5. A composition according to Claim 4, in which the nucleic acid sequence to be transferred is a genomic DNA, a cDNA, a messenger RNA or an oligonucleotide.

6. A composition according to Claim 5, wherein the vector comprises a sense sequence to be provided to a target cell in order to exert a function.

7. A composition according to Claim 6, in which the vector comprises an anti-sense sequence to be provided to a target cell in order to inhibit the functioning of a nucleic acid present in the target cell.

8. A composition according to any one of Claims 1 to 7, in which the vector is a liposome.

9. A composition according to any one of Claims 1 to 8, in which the vector is a virus.

10. A composition according to any one of Claims 1 to 9, in which the virus is an adenovirus, an adeno-associated virus, a herpes virus or a retrovirus.

11. A composition according to Claim 9, in which the virus is a replication-defective adenovirus.

12. A composition according to Claim 11, where the virus is a replication-defective adenovirus comprising a promoter selected from the group consisting of respiratory syncytial virus promoter, cytomegalovirus promoter, adenovirus major late protein (MLP), VA1 pol III and b-actin promoters.

13. A composition according to Claim 11, wherein the vector is pAd.RSV, pAd.MLP or pAd.VA1.

14. A composition according o Claim 11, wherein the vector is Ad.RSV.aVEGF or Ad.VA1.aVEGF.

15. A composition according to any one of Claims 10 to 14, wherein the vector also comprises a polyandenylation signal sequence.

16. A composition according to Claim 15, wherein the polyadenylation signal sequence is the SV40 signal sequence.

17. A method of treatment of a pathological condition in a subject in need of such treatment, comprising the step of administering an effective dose of a composition according to any one of Claims 1 to 16 to said subject.

18. A method according to Claim 17, in which the composition is administered systemically by injection.

19. A method according to Claim 17, in which the composition is administered topically.

20. A method according to Claim 17, in which the composition is administered directly into the tissue to be treated.

21. A method of preparing a composition according to any one of Claims 1 to 16, comprising the step of binding a nucleic acid or vector to a hyaluronic acid or a derivative thereof, and isolating the thus-formed complex.

22. A composition for treatment of a retinal disease mediated by abnormal vascularization comprising

a) an anti-sense nucleic acid sequence directed against vascular endothelial growth factor (VEGF), and

b) hyaluronic acid,

together with a pharmaceutically-acceptable carrier.

23. A composition according to Claim 22, in which the anti-sense nucleic acid sequence is present in a vector comprising a nucleic acid sequence to be transferred into a target cell.

24. A composition according to Claim 23, in which the vector is a virus.

25. A composition according to Claim 24, in which the virus is an adenovirus, an adeno-associated virus, a herpes virus or a retrovirus.

26. A composition according to Claim 24 or Claim 25, in which the viral vector is a replication-defective recombinant virus.

27. A composition according to Claim 26, where the virus is a replication-defective adenovirus comprising a promoter selected from the group consisting of respiratory syncytial virus promoter, cytomegalovirus promoter, adenovirus major late protein (MLP), VA1 pol III and b-actin promoters.

28. A composition according to Claim 27, wherein the vector is pAd.RSV, pAd.MLP or pAd.VA1.

29. A composition according to Claim 27, wherein the vector is Ad.RSV.αVEGF or Ad.VA1.αVEGF.

30. A composition according to any one of Claims 1 to 29, wherein the vector also comprises a polyadenylation signal sequence.

31. A composition according to Claim 30, wherein the polyadenylation signal sequence is the SV40 signal sequence.

32. A composition for treatment of a retinal disease mediated by abnormal vascularization, comprising an anti-sense nucleic acid sequence corresponding to at least a part of the sequence encoding VEGF, and optionally further comprising one or more adjuvants for increasing cellular uptake, together with a pharmaceutically-acceptable carrier.

33. A composition according to Claim 32, comprising as adjuvant hyaluronic acid or a derivative thereof.

34 [33]. A composition according to Claim 32 or Claim 33, wherein the anti-sense sequence has 100% complementarity to a corresponding region of the gene encoding VEGF.

35 [34]. A composition for short-term treatment according to Claim 32 or Claim 33, wherein the anti-sense sequence is 16 to 50 nucleotides long.

36 [35]. A composition for short-term treatment according to Claim 32 or Claim 33 [34], wherein the anti-sense sequence is 16 to 22 nucleotides long.

37 [36]. A composition for short-term treatment according to Claim [35] 32 or Claim 33, wherein the anti-sense sequence is 16 to 19 nucleotides long.

38 [37]. A composition according to Claim 32 or Claim 33, wherein a modified oligonucleotide as herein defined is used, and the anti-sense sequence is 7

to 50 nucleotides long.

[38. A composition according to any one of Claims 32 to 37 wherein the adjuvant is hyaluronic acid or a derivative thereof.]

39. A composition for long-term treatment of a retinal disease mediated by abnormal vascularization, comprising a recombinant virus comprising an anti-sense nucleic acid sequence corresponding to at least part of the sequence encoding VEGF, together with a pharmaceutically-acceptable carrier, wherein the anti-sense sequence is between 20 nucleotides in length and the full length sequence encoding VEGF.

40. A composition according to Claim 39, further comprising as adjuvant hyaluronic acid or a derivative thereof.

41. A composition according to Claim 39, or Claim 40 wherein the anti-sense sequence is between 50 nucleotides long and the full length sequence of VEGF.

42 [41]. A composition according to any one of Claims [1 to 40] 22 to 41, wherein the VEGF sequence is that of VEGF from human retinal pigment epithelial cells or choroidal endothelial cells.

43 [42]. A composition for treatment of a retinal disease mediated by abnormal vascularization, wherein said treatment is effective for an indefinite period, comprising a virus comprising an anti-sense DNA corresponding to at least part of the sequence encoding VEGF, together with a pharmaceutically-acceptable carrier, wherein said virus is one capable of integrating the anti-sense sequence into the genome of the target cell.

44. A composition according to Claim 43, further comprising as adjuvant hyaluronic acid or a derivative thereof.

45 [43]. A composition according to Claim [42] 43 or Claim 44, wherein the virus is an adeno-associated virus.

46 [44]. A composition according to [Claim 42 or] Claim 43, Claim 44, or Claim 45, wherein the anti-sense sequence is between 20 nucleotides long and the full length sequence of VEGF.

47 [45]. A composition according to Claim 43, Claim 44, or Claim 45, wherein the anti-sense sequence is between 50 nucleotides long and the full length

sequence of VEGF.

48 [46]. A method of treatment of a retinal disease mediated by abnormal neovascularization, comprising the step of administering an effective amount of an anti-sense nucleic acid sequence corresponding to at least part of the sequence encoding VEGF into the eye(s) of a subject in need of such treatment, thereby to inhibit neovascularization.

49. A composition according to Claim 48, further comprising as adjuvant hyaluronic acid or a derivative thereof.

50 [47]. A method according to Claim [46] 48 or Claim 49, wherein the anti-sense sequence is 16 to 50 nucleotides long.

51 [48]. A method according to Claim [46] 48 or Claim 49, wherein the anti-sense sequence is 16 to 22 nucleotides long.

52 [49]. A method according to Claim [46] 48 or Claim 49, wherein the anti-sense sequence is 16 to 19 nucleotides long.

53 [50]. A method according to Claim [46] 48 or Claim 49, wherein a modified oligonucleotide as herein defined is used, and the anti-sense sequence is 7 to 50 nucleotides long.

54 [51]. A method of treatment of a retinal disease mediated by abnormal neovascularization, comprising the step of administering an effective amount of a composition according to any one of Claims 22 to [45] 47 to a subject in need of such treatment.

55 [52]. A method of treatment of a retinal disease mediated by abnormal neovascularization, comprising the step of administering a composition according to any one of Claims 39 to 42 [41] to the eye(s) of a subject in need of such treatment, thereby to inhibit neovascularization in the long term.

56 [53]. A method of treatment of a retinal disease mediated by abnormal neovascularization, comprising the step of administering an effective amount of a composition according to Claims 42 to 47 [45] into the eye(s) of a subject in need of such treatment, thereby to inhibit neovascularization for an indefinite period.

57 [54]. A method according to any one of Claims 48 to 56 [46 to 53], wherein the retinal disease is selected from the group consisting of age-related macular degeneration, diabetic retinopathy, branch or central retinal vein occlusion,

retinopathy of prematurity, rubeosis iridis and corneal neovascularization.

58 [55]. A method of promoting uptake of an exogenous nucleic acid sequence by a target cell, comprising the step of exposing the cell to the nucleic acid, or to a virus or vector comprising the nucleic acid, in the presence of a hyaluronic acid or a derivative thereof.

59 [56]. A method according to Claim 58 [55], in which the target cell is a phagocytic cell.

60 [57]. A method according to Claim 55 or Claim 59 [56], in which the nucleic acid and hyaluronic acid are administered together *in vitro*.

61 [58]. A method according to Claim 58 or Claim 59 [55 or Claim 56], in which the nucleic acid and hyaluronic acid are administered together *in vivo*.